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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/323,765	06/01/99	SCOTT M	259.006US1

EXAMINER	
HAYES,R	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/323,765	Applicant(s) Scott et al
	Examiner Robert C. Hayes	Group Art Unit 1647

☒ Responsive to communication(s) filed on *Jan 16, 2001*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-52* is/are pending in the application.

Of the above, claim(s) *27, 29, 30, and 32-52* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-26, 28, and 31* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims *1-52* are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5 & 9*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I (claims 1-26, 28 & 31) in Paper No. 12 is acknowledged. The traversal is on the ground(s) that "the two sets of claims... are classified in related breakdowns of the same subclass (93.1 and 93.7)", and that the Examiner's assertion that the methods... require physically and functionally distinct elements is clearly in error". This is not found persuasive because relatedness of subclasses is not a criteria for overcoming a restriction requirement, and because each of these methods of Group II alternatively require "mammals" and administration protocols, which are physically and functionally distinct from the cell compositions, and methods of producing such, of Group I. Moreover, in contrast to Applicants' assertions, the cell compositions of Group I can also be used to produce polypeptides following transfection of the cells with appropriate constructs, which is a distinct process that is different from Group II. Lastly, and in contrast to Applicants' assertions that "decreasing phagocytosis is also a method included within the generic process of avoiding *rejection of cells or tissue*", this subject matter is also correctly part of Group II (i.e., as it relates to nonelected claims 27, 29-30 & 32-52). These inventions are, therefore, patentably distinct, because they have acquired a separate status in the art *as shown by their different classification* and the non-coextensiveness of the search and examination for each group would constitute an undue burden on the examiner to search and consider each of these separable groups with their recognized divergent subject matter.

Therefore, Applicants' arguments are not persuasive. The requirement is still deemed proper and is therefore made FINAL.

Claims 27, 29-30 & 32-52 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 7. This application contains claims 27, 29-30 & 32-52 drawn to an invention nonelected with traverse in Paper No. 12. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Objections

2. Claims 14 & 31 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. (e.g., claim 21 is not a method).

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2-7, 9, 18-19, 23-25, 28 & 31 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 5,908,624. Although the conflicting claims are not identical, they are not patentably distinct from each other because the non-immunogenic cellular compositions, and methods of producing such, from 5,908,624 encompass the non-immunogenic cellular compositions, and methods of making such, of the instant claims; especially as it relates to claim 19.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15, 17-23, 28 & 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, base claims 1 & 13 are all directed toward "anuclear" cells, and therefore, cannot also be "nuclear", as recited in claims 18, 19, 20, 21, 22, 23, 28 & 31; thereby, being indefinite. Conversely, base claim 9 is directed toward "nuclear"

cells, and therefore, cannot also be "anuclear", as recited in claims 15 & 17. In other words, no proper antecedent basis also exists for these "said" cells.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 2-7, 18-21, 23-25, 28 & 31 are rejected under 35 U.S.C. 102(e) as being anticipated by Desai et al. (U.S. Patent 5,578,442).

Desai et al. teach non-immunogenic cell compositions, as well as methods to produce these compositions, in which non-ionic water soluble polymers (i.e., hydrophilic/biocompatible; col. 4, lines 15-31 & 40-54) are covalently attached to viable, nucleated, mammalian cells/tissue through free radical polymerization (i.e., col. 4, lines 40-54; col. 5, lines 13-26; as it relates to claims 2, 6-7, 18 & 24-25), in which substances, such as polysaccharides (e.g., dextran; as it relates to claim 10) or the polyalkylene glycol, PEG (i.e., as it relates to claim 8), are not toxic (i.e, col. 4, lines 15-31; as it relates to claims 3 & 5), and in which attachment to antigenic

determinants, as recited, inherently occurs, as does the property that these cells remain viable for over 96 hours (i.e., as it relates to claim 2); absent evidence to the contrary. In that no "by-products" from the free radical polymerization (i.e., especially as it relates to UV-crosslinking; col. 3, lines 57-61) reasonably exist or remain after washing the treated cells to remove non-reacted hydrophilic polymers, the limitations of claim 4 are met. In that free radical/covalent attachment of polycationic/anionic linkage species are also disclosed (e.g., cols. 4-5 for polycationic species; col. 5-6 for anionic species), the limitations of claims 7 & 24-25 are met. Finally, nucleated cell compositions, and methods of producing such, include islets (i.e., as it relates to claim 22), hepatocytes and neuronal cells (col. 5, lines 27-33; as it relates to claims 20-21 & 31), "secreting cells" (i.e., vascular endothelial cells; as it relates to claims 22 & 19), as well as the epithelial cells contained in Desai's "cells having a modified surface" (i.e., col.4, line 47; col. 5, lines 27-37; as it relates to claim 23), which are further normally "part of a tissue or organ" (i.e., as it relates to claim 28).

6. Claims 1, 4-5, 7-8, 10-16, 24 & 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Francis et al. (WO 95/06058).

Francis et al. teach non-aggregating, non-immunogenic, anuclear and viable mammalian erythrocyte compositions (i.e., red blood cells) through covalent attachment of the polyalkylene glycol, TMPEG, as well as methods to produce these compositions (pgs. 64-65, Example 7; as it relates to claims 1, 7-8, 13-16, 24 & 26), in which polyalkylene glycols are not toxic at the

concentrations used (pgs. 14 & 52), as evidenced by no disruption of the cell membrane (i.e., pgs. 64-65; as it relates to claim 5), and in which no "by-products" from the covalent attachment of PEG reasonably exist or remain after washing the treated cells to remove non-reacted PEG moieties (i.e., as it relates to claim 4). Francis further teach that covalent attachment of other polymers, such as dextran and ficoll (pg. 33; as it relates to claims 10-11) and arabinogalactan (pg. 32; as it relates to claim 12) can be used to improve pharmacological properties of target molecules (pgs. 14 & 52).

7. Claims 1, 4-5, 7-8, 14-16, 24 & 26 are rejected under 35 U.S.C. 102(a) as being anticipated by Jeong et al. (1996).

Jeong et al. teach non-aggregating, non-immunogenic, anuclear and viable mammalian red blood cell compositions through covalent attachment of the polyalkylene glycol, MPEG, as well as methods to produce these compositions (pgs. 503-505; as it relates to claims 1, 7-8, 14-15, 24 & 26), in which polyalkylene glycols are not toxic at the concentrations used, as evidenced by the oxygen equilibrium studies disclosed (i.e, pgs. 505 & Fig. 4; as it relates to claim 5), and in which no "by-products" from the covalent attachment of PEG reasonably exist or remain after washing the treated cells to remove non-reacted PEG moieties (i.e., pg. 504-505; as it relates to claim 4).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-26, 28 & 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Desai et al., in view of Francis et al. (WO 95/06058).

Desai et al. is as set forth above for claims 2-7, 18-21, 23-25, 28 & 31. However, Desai do not specifically disclose non-immunogenic cellular compositions comprising anuclear cells/red blood cells, or methods of producing such.

Francis et al. is as set forth above for claims 1, 4-5, 7-8, 10-16, 24 & 26. Francis also teach covalent attachment of PEG derivatives, such as TMPEG and methoxypolyethylene glycol (pgs. 64, Example 7; pg. 31; as it relates to claim 9), as well as how covalent attachment of other polymers, such as dextran and ficoll (pg. 33; as it relates to claims 10-11) and arabinogalactan (pg. 32; as it relates to claim 12) can be used to improve pharmacological properties of target

molecules (pgs. 14 & 52). However, Francis do not teach covalent attachment of PEG derivatives, or other polymers, to nuclear cell surfaces.

It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to include Francis' red blood cells (RBCs), and alternate methods of covalently attaching other non-immunological polymers to cells, in Desai's non-immunological cell compositions, because of the common problems of non-compatible antigenic sites between different species/individuals for both nuclear and anuclear cells (i.e., RBCs and platelets), especially if such tissue/blood is scarce, and because Desai et al. disclose in their Detailed Description of the Invention that "[t]he process of the present invention can be used for rendering non-immunogenic *any* cell, tissue, organ, or system of organs, and the like, that may be used for transplant or the like" [emphasis added] (col. 6, lines 15-18); thereby, providing the motivation for using any cell type, including RBCs and platelets (i.e., as it relates especially to claims 15-23, 26 & 28) as a substrate for making non-immunogenic cell compositions.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Thursday, and alternate Fridays, from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

RCH

Robert C. Hayes, Ph.D.
April 4, 2001

Gary L. Kunz

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